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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,864	10/27/2005	Peter David Davis	3963.1001-000	3397

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HAMILTON, BROOK, SMITH & REYNOLDS, P.C.
530 VIRGINIA ROAD
P.O. BOX 9133
CONCORD, MA 01742-9133

EXAMINER	
LAU, JONATHAN S	

ART UNIT	PAPER NUMBER
4173	

MAIL DATE	DELIVERY MODE
11/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,864	DAVIS ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24,26-28 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-24,26-28 and 30* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Restriction Requirement

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

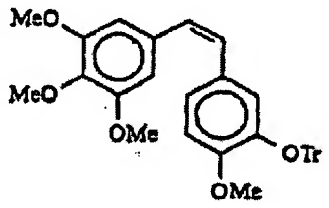
In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-23, drawn to a compound of formula (1) and pharmaceutical compositions thereof.

Group II, claim(s) 24 and 26-28, drawn to a method of ameliorating a proliferative disorder comprising administering said compound.

Group III, claim(s) 30, drawn to a method of ameliorating a proliferative disorder comprising administering said compound and a reductase, an anti-body reductase conjugate, a macromolecule-reductase conjugate or DNA encoding a reductase gene.

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The common feature of Groups I-III is the compound of formula (1). However, a compound of formula (1) is a known compound, for example disclosed by Seyedi et al. (WIPO publication WO 02/06279, provided by Applicant as document B2 in IDS filed 26 Sep 2005) as



Compound III

compound III on page 18, , a where Tr is trityl and "includes unsubstituted trityl ... and singly or multiply (one to five groups) substituted aryl groups on the trityl [group]; the group(s) attached to the aryl ring in the trityl [group] may be lower alkyl, lower alkoxy, fluorine and nitro" (Seyedi et al. spanning page 16, lines 23-28 and page 17, line 1). This corresponds to the instant formula (1) wherein Dr is combretastatin A4, X is a single covalent bond, n is 0, R1 and R2 are aryl, and Ar is a

nitro substituted aryl group. Therefore a compound of formula (1) does not serve as a single general inventive concept. The special technical feature of Group I is the specific chemical structure of the specific compound. The special technical feature of Group II is the specific method of treatment using a compound with a specific chemical structure. The special technical feature of Group III is the specific method of treatment using combination of a compound of formula (1) with a specific chemical structure and a reductase, an anti-body reductase conjugate, a macromolecule-reductase conjugate or DNA encoding a reductase gene.

Species Election Requirement

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1. In addition to restricting to the invention of Group I, II, or III, Applicant is required to elect from the following first species election below. If Applicant restricts to the invention of Group II or III, Applicant is further required to elect from the following second species election below.

First species election

The species are the specific chemical structures of compounds encompassed by the genus of formula (1), for example disclosed in claim 22, as follows:

1-(4-Methoxy-3-(2-(5-nitrothiophen-2-yl) propan-2-yl)oxyphenyl-2-(3,4,5-trimethoxy)phenyl-Z-ethene,

1-(4-Methoxy-3-(2-(4-nitrophenyl)propan-2-yl) oxyphenyl-2-(3,4,5-trimethoxy)phenyl-Z-ethene,

9-(7,8-Dihydroxy-2-methyl-hexahydro-pyrano[3,2-d][1,3]-dioxin-6-yloxy)-5-{3,5-dimethoxy-4-[1-methyl-1-(4-nitrophenyl)-ethoxy]-phenyl}-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho[2,3-d][1,3]dioxol-6-one,

6-(2-(4-nitrophenyl)propan-2-ylsulfanyl)-9H-purine,

1-(4-Methoxy-3-(1-methyl-4-(5-nitrothien-2-yl)piperidin-4-yl)oxycarbonyloxy)phenyl-2-(3,4,5-trimethoxy)phenyl-Z-ethene,

1-(4-Methoxy-3-(2-(1-methyl-2-nitroimidazol-5-yl) propan-2-yl)oxyphenyl-2-(3,4,5-trimethoxy)phenyl-Z-ethene,

6-(2-(5-nitrothien-2-yl)propan-2-ylsulfanyl)-9H-purine,

N^4-(2-(5-nitrothien-2-yl) prop-2-yl)oxycarbonyl-1-β-D-arabinofuranosylcytosine,

1-(3-(1-Ethoxycarbonyl-1-(5-nitrothien-2-yl)ethoxy)-4-methoxy-phenyl)-2-(3,4,5-trimethoxyphenyl)-Z-ethene, and

N-(2-{3-[1-Methyl-1-(5-nitro-thiophen-2-yl)-ethoxy]-phenyl}-ethyl)-acetamide.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims

are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The claims are deemed to correspond to the species listed above in the following manner:

All claims are generic to the compound of formula (1).

If Applicant restricts to the invention of Group II or III, Applicant is further required to elect from the following second species election below.

Second species election

The species are the specific diseases treated by the compound encompassed by the genus of formula (1), for example disclosed in claims 26, 27, and 28, as follows:

cancer other than a solid tumor or leukemia,

rheumatoid arthritis,

psoriatic lesions,

diabetic retinopathy,

wet age-related macular degeneration,

hypoxic disorder,

a solid tumor, and

leukemia.

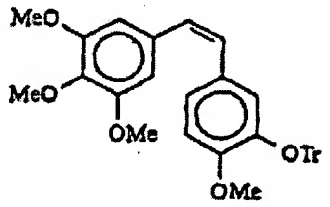
Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are

generic is considered non-responsive unless accompanied by an election. Applicant is cautioned that election of a subgenus, such as "cancer", will be considered non-responsive.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The claims are deemed to correspond to the species listed above in the following manner:
Claims 26, 28, and 30 are generic to the disease treated by said compound.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: A compound of formula (1) is a known compound, for example disclosed by Seyedi et al. (WIPO publication WO 02/06279, provided by Applicant as document B2 in IDS filed 26 Sep 2005) as



Compound III

compound III on page 18, , a where Tr is trityl and "includes unsubstituted trityl ... and singly or multiply (one to five groups) substituted aryl groups on the trityl [group]; the group(s) attached to the aryl ring in the trityl [group] may be lower alkyl, lower alkoxy, fluorine and nitro" (Seyedi et al. spanning page 16, lines 23-28 and page 17, line 1). This corresponds to the instant formula (1) wherein Dr is combretastatin A4, X is a single covalent bond, n is 0, R1 and R2 are aryl, and Ar is a nitro substituted aryl group. Therefore a compound of formula (1) does not serve as a single general inventive concept. The special technical feature of Group I is the specific chemical structure of the specific compound. The special technical feature of Group II is the specific method of treatment using a compound with a specific chemical structure. The special technical feature of Group III is the specific method of treatment using

combination of a compound of formula (1) with a specific chemical structure and a reductase, an anti-body reductase conjugate, a macromolecule-reductase conjugate or DNA encoding a reductase gene.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder.

All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Ardin Marschel can be reached on 571-272-0718 or Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JSL